Jazz Pharmaceuticals

www.JazzPharmaceuticals.com

Submitted by
Francois Di Trapani, Vice President Global Scientific Affairs
Jazz Pharmaceuticals
3170 Porter Drive
Palo Alto, CA 94304
Phone: 650.496.2759
Email: francois.ditrapani@jazzpharma.com

Date of Request: 06/15/2020

Notification of FDA approval of Zepzelca™ (lurbinectedin) for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on after platinum-based chemotherapy.

As a follow-up to Jazz Pharmaceutical's request on 04/29/2020,[1] it is my pleasure to notify the NCCN SCLC Panel that lurbinectedin has been approved by the FDA on 06/15/2020 based on the registrational study.[2,3] Separately results from a pooled safety analysis are now available comparing the safety of lurbinectedin with topotecan.[4]

Specific Changes: Please consider adding lurbinectedin:

SCL-E 2 of 4: SCLC Subsequent Systemic Therapy

- "Relapse ≤6 months": Lurbinectedin under "Preferred Regimen"
- "Relapse >6 months": Lurbinectedin as Preferred Regimen

FDA Approval: Lurbinectedin is an alkylating drug indicated for the treatment of adult patients with metastatic small cell lung cancer (SCLC) with disease progression on or after platinum-based chemotherapy.
This indication is approved under accelerated approval based on overall response rate and duration of response. Continued approval for this indication may be contingent upon verification and description of clinical benefit in a confirmatory trial(s).

Rationale: Relapsed SCLC remains a significant unmet need as prognosis is poor after failure of initial therapy.[5] In SCLC patients treated with lurbinectedin after initial platinum-based chemotherapy with or without immunotherapy, clinical responses were observed both in patients who were chemo-sensitive and chemo-resistant, without the use of granulocyte colony-stimulating factors (G-CSF) as primary prophylaxis.[3]

Supporting Literature: The registrational phase 2 study included 105 patients with SCLC treated with one prior chemotherapy-containing line, including patients with prior exposure to immunotherapy.[3] Extensive stage disease at diagnosis was evident in 73 (69.5%) patients. Treatment consisted of lurbinectedin 3.2 mg/m^2 administered as a 1-hour intravenous infusion every 3 weeks. Primary prophylaxis with G-CSF was not allowed. At a median follow-up of 17.1 months, overall response rate (ORR) the primary endpoint of the trial was 35.2%. Responses were observed in both chemo-sensitive (ORR 45.0%) and chemo-resistant (ORR 22.2%) cases. Chemo-resistant disease was defined as chemotherapy-free interval (CTFI) less than 90 days, including a subgroup of 21 patients of very poor prognosis with CTFI less than 30 days. Median duration of response was 5.3 months. Median

progression-free survival and overall survival (OS) in the overall population was 3.5 months and 9.3 months, respectively. Among SCLC patients who had an initial objective response, median OS was 12.6 months in the overall population, 15.8 months in the chemo-sensitive group, and 10.9 months in the chemo-resistant group.[3]

In an exploratory analysis of patients with CTFI greater than 6 months (n=20), ORR was 60%, median OS was 16.2 months, and 24-month OS was 27.1%. Further systemic treatment was administered in 73% of patients after lurbinectedin discontinuation; 55% received platinum-based chemotherapy and 20.5% received immunotherapy.[6] (*Important Note: These data in the preceding sentence are subject to embargo. As such, they are not in the public domain and are expected to be treated as confidential by NCCN and its members and may not be discussed or disclosed outside of this review panel. Jazz will notify NCCN when the data are in the public domain).*

The most common adverse events in the study were neutropenia (71.4%; grade 3/4, 45.7%); febrile neutropenia (4.8%), fatigue (58.1%; grade 3, 6.7%), decreased appetite (21.0%), nausea (32.4%) and vomiting (18.1%).[3] Primary prophylactic G-CSF was not allowed, and only 21.9% patients received G-CSF as secondary prophylaxis or therapeutic treatment for neutropenia. Serious treatment-related adverse events occurred in 10.5% of patients. Only two patients (1.9%) discontinued lurbinectedin due to treatment-related adverse events. No treatment-related deaths were reported.[3]

A pooled safety analysis was conducted comparing the safety of lurbinectedin with topotecan, including data from 554 patients treated with lurbinectedin for SCLC (N=105, Phase II BASKET study SCLC subset), ovarian cancer (N=219, Phase III CORAIL study), and other solid tumors (N=230, Phase II BASKET study), and 87 patients treated with Topotecan (Phase III CORAIL study). [4]

With the limitations of indirect comparisons, in the pooled safety analysis, fewer lurbinectedin-treated patients had severe hematological toxicities, SAEs, dose adjustments, treatment discontinuations and use of supportive treatments than topotecan-treated pts. [4]

Sincerely,

References:

1. Jazz Pharmaceuticals. Submission request to NCCN. [04/29/2020] **(enclosed)**
2. Jazz Pharmaceuticals. [Zepzelca™] [Prescribing Information]. Jazz; 2020. **(enclosed)**
3. Trigo J, et al. Lurbinectedin as Second-line Treatment for Small Cell Lung Cancer Patients: Results from a Single-arm Phase 2 Study. *Lancet Oncology*. 2020;21(5):645-654. **(enclosed)**
4. Leary A, et al. Pooled Safety Analysis of Single-agent Lurbinectedin Versus Topotecan (Results From a Randomized Phase III Trial CORAIL and a Phase II Basket Trial). *Journal of Clinical Oncology*. 2020;38(suppl): Abstract 3635. **(enclosed)**
5. NCCN Clinical Practice Guidelines in Oncology. Small Cell Lung Cancer. V3.2020.
6. Subbiah V, et al. Activity of Lurbinectedin in Second-line SCLC Patients Who Are Candidates for Platinum Re-challenge. **Data on file, subject to embargo.**